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09/578,900	05/26/2000	John P. Carulli	032796-019	8399

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ANGELL, JON E

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/578,900	Applicant(s) CARULLI ET AL.	
	Examiner J. Eric Angell	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *3-5 and 8-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Notice to comply

DETAILED ACTION

Claims 1-47 are pending in the application.

The amendment filed 8/12/02 has been entered.

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1, 2, 6 and 7) and the species SEQ ID NO:1, in Paper No. 16 is acknowledged. The traversal is on the ground(s) that (1) There is not a serious search burden in first and second restriction requirements, (2) No reason set forth indicating why inventions (subgroups) are independent or distinct, (3) Inconsistent with MPEP 2173.05(h), (Markush groups).

2. This is not found persuasive because: (1) The original restriction indicated that the Groups were independent and distinct and searching the different groups would pose a serious search burden because the searches would encompass different search strategies wherein different subject matter is searched using different search terms and the searches would require searching different classifications. Therefore a serious search burden does exist. (2) The subgroups of species of nucleic acid molecules (i.e. SEQ ID NOS.) are independent and distinct and a serious search burden does exist to search all species subgroups. First, as indicated in the previous Office Action, the different molecules are structurally and functionally distinct. They are structurally distinct because each molecule comprises a different nucleotide sequence. They are functionally distinct because each polymorphism confers a different phenotype as indicated by the different phenotype of the wild-type molecule (Zmax1) and the polymorphism known as HBM (see pg. 10 of the specification which indicates individuals with the HBM polymorphism

have lower LDL, triglycerides and VLDL concentrations, and higher HDL concentrations). Thus each polymorphism would likely have a different function when used in a method. For instance, the different molecules would have different specificities for the binding molecules, or may identify different binding molecules. Therefore, the subgroups of species have distinct functions as well as distinct structures. It appears that Applicant is arguing that the subgroups are not patentably distinct (see page 4, second full paragraph and pages 5 and 6 of the response filed 8/12/02). If the subgroups are not patentably distinct as claimed, applicant should clearly admit on the record that this is the case. Furthermore, a serious search burden exists to search the different subgroups of species because the searches would require multiple queries of the sequence databases and the consideration of all of the articles and database submissions that are identified in the search. (3) The restriction is appropriate because the subgroups of species are structurally, functionally, and patentably distinct for the reasons set forth above and is appropriate to restrict molecules (and methods of using molecules) that are patentably distinct, regardless if they are listed in a single claim, such as in Markush group form.

Therefore, the requirement is still deemed proper and is therefore made FINAL.

Claims 3-5 and 8-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 17 (filed 8/12/02).

Claims 1, 2, 6 and 7 are examined herein.

Drawings

3. New corrected drawings are required in this application because the margins of the figures are incorrect (e.g., see Figures 1, 3, 5, 10, 11 and 12). Also see attached form PTO-948 (Draftperson's Drawing review). Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically the application contains sequence disclosures which are not designated with the appropriate sequence identifiers (SEQ ID NO.). For instance, see Figures 3 and 6; and pages 75, 77 and 83 of the specification).

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) in response to this action. Failure to comply with these requirements will result in

ABANDONMENT of the application under 37 CFR 1.821(g). Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Priority

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e) and 120 and/or 121 is acknowledged. However, the provisional applications upon which priority is claimed (60/071449 and 60/105511) fail to provide adequate support under 35 U.S.C. 112 for claims 1, 2, 6 and 7 of this application. The provisional applications do not disclose the sequences of Zmax1, HBM, or the polymorphisms of Zmax1/HBM (i.e. the polymorphisms of Table 4) encompassed by the claims.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 indicates in step (A), "identifying a molecule which binds to SEQ ID NO: 1..." Step (B) indicates, "identifying a molecule which binds to SEQ ID NO: 2..." and Step (C) indicates, "comparing the extent of binding or the extent of inhibition of binding, of the molecule to each nucleic acid sequence..." This is confusing because Step (C) seems to indicate one molecule is identified in Steps (A) and (B) (i.e. the molecules of (A) and (B) are the same

molecule). However, as written steps (A) and (B) identify molecules which bind to SEQ ID NO: 1 and SEQ ID NO: 2, respectively. Therefore it is unclear what "the molecule" of step (C) is referring to. Specifically, it is unclear if "the molecule" of Step (C) is the molecule of (A) or the molecule of (B) or if the molecule of (A) and (B) are necessarily the same. Furthermore, claim 6 recites, "wherein the molecule that binds or inhibits binding, more or less to the nucleic acid sequence of SEQ ID NO: 2 or the nucleic acid sequence of SEQ ID NO: 1... is the candidate molecule." This recitation renders the claim indefinite because it is unclear if the molecule is binding more or binding less to SEQ ID NO: 2 or binding more or binding less to SEQ ID NO: 1; or inhibiting the binding more or inhibiting the binding less to SEQ ID NO: 2 than SEQ ID NO:1.

Claim 6 is also unclear because the recitation "a molecule that binds to or inhibits binding of a molecule..." (see steps A and B). This recitation renders the claim indefinite because it is unclear if the molecule binds or inhibits binding of itself or a different molecule. Amending the claim to recite "a first molecule the binds or inhibits the binding of a second molecule" would be more clear. Further more, amending step C of claim 6 to identify "the molecule" as either "the first molecule" or "the second molecule" would also make the claim clearer.

Furthermore, claim 6 refers to a polymorphism of Table 4. However, the exact sequences of the polymorphisms of Table 4 are unclear because the Table appears to refer to the sequences as Contig. Numbers (see Table 4). Identification of the polymorphisms with SEQ ID NOS. would be clearer.

Claim 7 depends upon claim 6 and is therefore rejected for the same reasons.

Claim Rejections - 35 USC § 112, first paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a method for identifying molecules that bind to HBM or Zmax1. However, the claims do not specifically recite the sequence of HBM or Zmax1, and the specification indicates that Zmax1 is the "wild-type" and that many polymorphisms of the wild-type exist, including all of the polymorphisms of Table 4 (and including HBM). Therefore, without a clear indication of the sequences of Zmax1 and HBM (such as with SEQ ID NO), the claims encompass any polymorphism of Zmax1 or HBM.

Therefore, the instant claims encompass sequences which are different from those disclosed in the specific SEQ ID NOS: 1 and 2, and include variants and polymorphisms for which no written description is provided in the specification. This large genus is represented in the specification by only the named SEQ ID Nos. Thus, applicant has express possession of only about 25 polymorphisms (see Table 4), in a genus which comprises hundreds of millions of different possibilities, considering every possible variant or polymorphism, including all possible single nucleotide substitutions encompassed by the claims.

The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or

features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet the functional limitations is provided (the functional limitation that the polymorphism is involved in lipid regulation).

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that:

> "In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

> It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that: "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only certain, specific polymorphisms are described (i.e., specific SEQ ID NOS.).

Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of every possible polymorphism other than those expressly disclosed which represent functional polymorphisms of Zmax1, which are involved in lipid regulation. Therefore, the claims fail to meet the written description requirement by encompassing polymorphisms for which no description is provided in the specification.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dong et al. (Biochem. Biophys. Res. Com. 251:784-790; 1998) in view of Fields et al. (US Patent 5,283,173; 1994).

The instant claims are drawn to a method for identifying a molecule involved in lipid regulation comprising identifying a molecule that binds to, or inhibits the binding of molecule to HBM or Zmax1; wherein the molecule is a protein. It is noted that, as stated above the claim encompasses using any variant or polymorphism of Zmax1 or HBM.

Dong teaches the isolation of a molecule (LR3) that is 99.4% identical to HBM (SEQ ID NO: 2). Therefore Dong teaches a molecule that is encompassed by the claims. Dong teaches that LR3 is a member of the LDL receptor family of proteins and that the LDL family of receptors are known to function in the endocytosis of plasma lipoprotein and cholesterol homeostasis and are involved in lipid metabolism (see p. 784, abstract and column 2 and attached sequence alignment).

Dong does not teach a method for identifying molecules involved in lipid regulation by identifying molecules that interact with LR3.

Fields teaches a method for identifying proteins that interact with each other in vivo. Specifically, Fields teaches a method wherein a first protein is expressed as a fusion with a DNA-binding domain of a transcriptional activator and a second protein of interest is expressed as a fusion with a transcriptional activation domain. When this system is used and the first and

second fusion proteins interact, the interaction of the complex of fusion proteins activates the expression of a selectable marker gene, thus indicating that the two proteins of interest interact (see, e.g. abstract and column 4). Fields also teaches that the method can be used to test the interaction of a multiplicity of proteins, such as those encoded by the entire genome of a cell (see column 3, second paragraph). Field specifically teaches that the second hybrid protein may be encoded on a library of plasmids that contain genomic, cDNA, or synthetically generated DNA sequences encoding the transcriptional activation domain (see column 5, lines 1-8), thus indicating that the method can be used to identify proteins that interact with a protein wherein a library of fusion proteins are expressed in a cell with a fusion protein of interest.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Dong with Fields to create a method for identifying molecules that are involved in lipid regulation by using the method of Fields wherein the first protein of interest is LR3 and the test proteins are produced from a library of possible proteins with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Dong, who teaches that LR3 is member of the LDL receptor family of proteins, a family of proteins known to be involved in lipid regulation. Therefore, identifying regulators of LR3 would identify potential regulators of lipid regulation.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
October 1, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER